PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 43182-0006	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/CA2004/001893	International filing date *(day/month/year)* 29 October 2004 (29-10-2004)	Priority date *(day/month/year)* 29 October 2003 (29-10-2003)

International Patent Classification (IPC) or national classification and IPC
IPC: G06F 19/00 ***(2006.01)*** , G06F 17/20 ***(2006.01)***

Applicant
TRIALSTAT CORPORATION ET AL

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [ ] *(sent to the applicant and to the International Bureau)* a total of 7 sheets, as follows:
      [ ] sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. 1 and the Supplemental Box.
   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - [X] Box No. I Basis of the report
   - [ ] Box No. II Priority
   - [X] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - [ ] Box No. IV Lack of unity of invention
   - [X] Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - [ ] Box No. VI Certain documents cited
   - [ ] Box No. VII Certain defects in the international application
   - [X] Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29 August 2005 (29-08-2005)	9 March 2006 (09-03-2006)
Name and mailing address of the IPEA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer Kristina Deczky (819) 934-4156

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

[X] the international application in the language in which it was filed

[ ] a translation of the international application into , which is the language of a translation furnished for the purposes of:

[ ] international search (Rules 12.3(a) and 23.1(b))

[ ] publication of the international application (Rule 12.4(a))

[ ] international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

[ ] the international application as originally filed/furnished

[X] the description:

[ ] pages — as originally filed/furnished

[ ] pages* 15-17 and 22 — received by this Authority on 29 August 2005

[ ] pages* — received by this Authority on

[X] the claims:

[ ] pages — as originally filed/furnished

[ ] pages* — as amended (together with any statement) under Article 19

[X] pages* 28-30 — received by this Authority on 29 August 2005

[ ] pages* — received by this Authority on

[ ] the drawings:

[ ] pages — as originally filed/furnished

[ ] pages* — received by this Authority on

[ ] pages* — received by this Authority on

[ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [X] The amendments have resulted in the cancellation of:

[ ] the description, pages

[X] the claims, Nos. 2, 13, 17, and 18

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

[ ] the entire international application

[X] claims Nos. 1-8 and 10-20

because:

[ ] the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify):*

[ ] the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify):*

[ ] the claims, or said claims Nos. are so inadequately supported
by the description that no meaningful opinion could be formed *(specify):*

[ ] no international search report has been established for said claims Nos.

[ ] a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

[ ] furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

[ ] a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[X] See Supplemental Box for further details.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-20	YES
	Claims	None	NO
Inventive step (IS)	Claims	1-6, 10-13, 15, and 17	YES
	Claims	8, 9, 14, 16, and 18-20	NO
Industrial applicability (IA)	Claims	9	YES
	Claims	None	NO

2. Citations and explanations (Rule 70.7)

D1: GB 2 359 645 (Brooke et al) 29 August 2001 (29-08-2001)

D2: Tornqvist et al, "XML and objects-the future of the e-forms on the Web,"Enabling Technologies: Infrastructure for Collaborative Enterprises, 1999. (WET ICE '99) Proceedings. IEEE 8th International Workshop , vol., pp.303-308, 1999

D3: Fan et al, "FormPlus: a form authoring toolkit," Computer Software and Applications Conference, COMPSAC 90. Proceedings., Fourteenth Annual International , vol., no.pp.255-260, 31 Oct-2 Nov 1990

Novelty

D1 considered to be the closest prior art discloses a method of generating a form using an XML file detailing the data and structure of an XML document using a computer system by generating a script with control statements detailing the structure of the document, processing the script using a script processor, and generating the document using the information specified by the control statement. The XML document is converted into an output document for a display. However, D1 does not disclose generating a patient form or a retrieving an XML file from a computer readable medium. Therefore claims 1-20 meet the requirements for novelty as set out in PCT Article 33(2).

Inventive Step

Claim 1 does not meet the requirements for inventive step as set out in PCT Article 33(3) in light of the teachings of D1 and common general knowledge in that art.

Regarding claim 1, D1 discloses a method of generating an XML document using a computer system by generating a script with control statements detailing the structure of the document, processing the script using a script processor, and generating the document using the information specified by the control statement, converting the XML document into an output document for a display (see page 4 line 25-page 5 line 8, claims 1 and 3). D1 differs from claim 1 in that D1 does not disclose retrieving an XML file from a computer-readable medium (D1 retrieves the scripts from a central database) or the form being a patient form. However, whether a file is stored on a computer readable medium or in a database is a design choice. It is well known in the art that XML is a markup language that uses elements to define the layout of a document, questionnaire or form. A person skilled in the art would be able to program the file to output a form for any application, be it business or healthcare. Therefore creating a patient form using the method disclosed in D1 does not involve an inventive step.

Claims 2-6 do not meet the requirements for inventive step as set out in PCT Article 33(3) in light of the teachings of D1, D2, and common general knowledge in that art.

(continued on supplemental sheet)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

On page 26 lines 12-15 there is an appendix incorporated by reference. As stated in PCT Guidelines paragraph 148, PCT makes no provisions for appendices in the international application. If the files are intended to be part of the application they should be printed from the CDROM on which they were submitted and numbered to comply with Section 207 under a heading which makes their status clear.

Claim 10 does not comply with *PCT Article 6* as "said patient form" lacks antecedent.

Claim 14 does not comply with *PCT Article 6* as the second introduction (use of an indefinite article) of an element already introduced causes ambiguity. The term "a patient form" has been defined previously in the claims. The aforementioned term should therefore be referred to using a definite article.

There is a typographic error in claim 5 line 2 "neeed" should be "needed".

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box III

The subject matter of claims 1-8 and 10-20 pertain to a computer program and computer program product which may be considered excluded subject matter in certain jurisdictions according to PCT Rule 67.1(iv). No unified criteria exists under PCT for assessing the industrial applicability of computer program and computer product claims. Thus no opinion has been provided with regards to industrial applicability.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Regarding claims 2-4 and 6, XML is a markup language that can easily generate any form (see D2 page 4 paragraph under the heading Library Service Hours Form). Therefore taking known forms and using computer software to make them available electronically does not involve an inventive step.

Regarding claim 5, D2 discloses having the XML questionnaire validate or verify the responses entered by the user to ensure proper data is acquired from the user (see Software Support for XML E-forms and page 4 column 1 paragraph 2). D2 differs from that disclosed in claim 5 as D2 does not disclose transmitting patient information and using the patient information to verify the eligibility of a patient and if eligible then generating a randomization code for a patient and for use in a clinical trial. It is well known in the art that patients are screened for eligibility into clinical trials and randomized to treatment or placebo groups for the experiment without regard to any patient characteristics or study personnel desires or biases. This has traditionally been done by having the patient answer a questionnaire and then a person will determining his or her edibility. Simply automating this process by use of a computer to fill out the criteria, determine the patient's eligibility, and giving him or her a randomization code does not involve an inventive step.

Claims 10-13 do not meet the requirements for inventive step as set out in PCT Article 33(3) in light of the teachings of D1 and common general knowledge in that art.

Regarding claim 10, D1 discloses a computer program product for installation in a central computer system connected to the Internet (see Figure 1 and see page 4 line 25-page 5 line 8, claims 1 and 3) code for generating a form defined by an XML file. D1 differs from claim 10 in that the form is not defined to be a patient form. However, as discussed above in claim 1, XML is a markup language that uses elements to define the layout of a document, questionnaire or form. A person skilled in the art would be able to program the file to output a form for any application, be it business or healthcare. Therefore creating a patient form using the method disclosed in D1 does not involve an inventive step.

Regarding claims 11-13, XML is a markup language that can easily generate any form (see D2 page 4 paragraph under the heading Library Service Hours Form). Therefore taking known forms and making them using a computer product containing software to generate forms to make them available electronically does not involve an inventive step.

Claim 15 does not meet the requirements for inventive step as set out in PCT Article 33(3) in light of the teachings of D1, D3, and common general knowledge in that art.

Regarding claim 15, software programs that do not require any programming knowledge to create forms are well known (see D3 abstract). Therefore creating a form for a specific application (a patient form) without expert knowledge of computer programming does not involve an inventive step.

Claim 17 does not meet the requirements for inventive step as set out in PCT Article 33(3) in light of the teachings of D1, D2, and common general knowledge in that art.

Regarding claim 17, D2 discloses hiding and revealing questions on a form and having rules of what order the form needs to be filled in (see page 4 column 1 paragraph 4 and page 4 under the heading Advantages over HTML second bullet).

Industrial Applicability

The subject matter of claim 9 meets the requirements for industrial applicability as set out in PCT Article 33(4).

The subject matter of claims 1-8 and 10-20 pertain to a computer program and computer program product which may be considered excluded subject matter in certain jurisdictions according to PCT Rule 67.1(iv). No unified criteria exists under PCT for assessing the industrial applicability of computer program and computer product claims therefore no opinion with regards to industrial applicability has been provided.

Internet Information Server 104, telephone interactive voice response (IVR) 105 and PDA interface means 106. Input to the central computer system 100 can be, depending on the platform, at least one of mouse 112, keyboard 114, telephone keypad 120 and input means of PDA 124. Output from the IIS 104 can be communicated to the user by display 110. Output from the IVR system 105 can be communicated to the user by telephone speaker 118. Output from the interface means 106 can be communicated to the user by the display of the PDA 124.

Because the clinical analytics system can automatically generate and deploy code for the eCRF to various platforms, once the form is authored or updated, investigators can have their new forms deployed to the field within minutes on both Palm™ and Web platforms. This represents a very significant time savings to investigators.

Making changes to and redeploying CRFs and eCRFs can be a large contributor to the operation cost of deploying a clinical trial. Trial sites (typically hospitals) tend to be geographically dispersed which complicates the distribution of updated forms in addition to the problem of assuring that all sites are using latest version forms. In less sophisticated electronic trial packages, changing electronic forms typically entails hand editing HTML and JavaScript® code, updating a database schema, recoding PDA software and having the sites update their installed software. This process can add months to the length of a clinical trial and can add a great deal of cost to the organization running it. The ability to quickly redeploy forms across all platforms can permit high cost savings as well as strategic and patient value in terms of completing trials more quickly. Also it can remove the risk that some investigators in the field may be working from outdated forms.

Randomization is one of the most critical activities in a clinical trial because this is what distinguishes it from less rigorous scientific methods. However, in clinical settings where nurses or research assistants need to

randomize a new patient for entry into a trial, being able to randomize quickly using a mobile device is an advantageous.

Handheld randomization, according to an embodiment of the invention, entails a PDA connecting to a remote randomization server through a secure Internet connection and getting the next randomization number/code. The preferred system implementing randomization also verifies that the potential participant meets all inclusion criteria and does not meet any exclusion criteria. This provides an additional protection mechanism to avoid ineligible patients being enrolled in a trial. In a preferred implementation of the randomization method using a PDA, the process typically takes less than a minute.

Figure 4 illustrates two possible methodologies for handheld randomization. A first methodology includes all of the illustrated steps. A second methodology omits steps 218 and 222.

At step 200, a uset Hotsyncs™ their Palm™ device, and a custom application is started on the randomization server.

At step 204, the server side database is populated with data from the palm based eCRFs.

At step 208, updated form information is sent back to the Palm™.

At step 212, steps 216 through 222 follow if the user has requested a randomization code or codes.

At step 216, a flag equating to a single data cell is transmitted and populated to the database.

At step 218, a second trigger associated with the randomization table is fired. The second trigger halts synchronization process until the new

randomization code is populated in the patient record (step 220). Once this has occurred the second trigger terminates.

The next time the user synchronizes their Palm™ (step 224), the newly populated randomization data is sent to the Palm™ (step 228), to allow the user to determine if the patient is included or excluded.

In alternative embodiments of the randomization process disclosed in this patent document, the process is implemented through a web interface or through an automated phone system. In settings where there is a wireless network, the handheld randomization method can provide a high degree of flexibility.

A description of a possible implementation of the telephone automated central randomization embodiment of the invention is described in Table M below:

TABLE M

	Automated Message (Pseudo-code in square brackets)	User Keypad Input
1.	You have reached the ABC Research Group Central Randomization Service.	
2.	Using the keypad on your touch-tone phone, please enter the study code followed by the # key.	13#
3.	[If they enter an invalid study code in 2: "Invalid study code, 2 (or 1) tries left" If they do this 3 times, "Your code seems to be invalid. Please double check your study code and call back later." -- EXIT --]	
4.	Please enter your authorization code followed by the # key.	12345#
5.	[If they enter an incorrect authorization code in 4: "Invalid authorization code, 2 (or 1) tries left" If they do this 3 times, "Your code seems to be invalid. Please double check your study code and authorization code and call back later." -- EXIT --]	
6.	Welcome to the VIP study. Please enter your center number followed by the # key.	01#

other errors will reduce data quality. For example, some forms could be missed altogether and this increases the chances that all data on that patient is wasted.

Because data is stored centrally, patient data can be tracked in real time both through the web and on the Palm™. This allows study coordinators to monitor recruitment rates much more closely that with manual systems. It also adds significantly to patient protection since adverse events or trends can be recorded, tracked and acted on in real time. Again, this is very difficult to do with traditional systems.

An embodiment of the clinical analytics system disclosed in this patent document includes a software suite providing features that make it much easier for a large team of investigators and coordinators to collaborate in the conduct of a clinical trial. One implementation of the software suite comprises a forum with a fine permission structure, a secure instant messaging system among trial managers, a document management system that allows the categorizing and archiving of documents, and a version control system that allows multiple people to collaborate in the production of a document.

From a trial's inception there are many documents that are shared among the trial managers and the investigators (the trial team). These can be drafts of the CRFs, drafts of the protocol, amendments, instructions to the sites, Research Ethics Board letters, and regulatory submissions. Some of these documents are sensitive and some are proprietary. Therefore, a secure way to collaborate and share this information from the inception of a trial is critical.

In the past the trial team exchanged documents by email. In addition to possible serious security problems that this entails, email does not easily control versions and stop multiple people from overwriting each other's work. Plus, email does not provide an audit trail. The same applies to discussions

WHAT IS CLAIMED IS:

1. A method comprising the steps of:

retreiving an XML file from a computer-readable medium, said XML file detailing data and structure of a patient form;

processing said XML file by running of an XML-responsive application;

generating said patient form defined by said XML file; and

displaying said patient form on a display.

2. The method according to claim 1, wherein said patient form is a screening form.

3. The method according to claim 1, wherein said patient form is a post-randomization form.

4. The method according to claim 1, wherein said patient form is a termination form.

5. The method according to claim 1, further comprising the steps of:

transmitting neeed patient information across a communications medium in order to process said patient information when both said patient information has been entered into said patient form and said patient form has been submitted;

using said patient information to verify eligibility of a patient; and

if eligibility of said patient is confirmed, generating a randomization code for said patient and for use in a clinical trial.

6. The method according to claim 5, wherein said patient form is a screening form.

7. The method according to claim 6, further comprising the step of storing said randomization code in a database within a central computer system.

8. The method according to claim 1, wherein said display is a personal digital assistant display.

9. A network comprising a plurality of nodes, one of said nodes being a central computer system, at least another of said nodes being a wirelessly enabled device in communication with said central computer system, at least yet another of said nodes being a personal computer in communication with said central communication system, and said nodes storing computer executable instructions for carrying out the method of claim 5.

10. A computer program product containing a software program for installation in a central computer system that is connected to a network, the software program comprising:

code for generating code for a patient form, said patient form defined by an XML file.

11. The computer program product according to claim 10, wherein said patient form is a clinical trial screening form.

12. The computer program product according to claim 10, wherein said patient form is a clinical trial post-randomization form.

13. The computer program product according to claim 10, wherein said patient form is a clinical trial termination form.

14. The computer program product according to claim 10, wherein said software program further comprises code for network deployment of said code for a patient form.

15. The computer program product according to claim 10, further comprising an XML form specification facilitating creation of said patient form.

16. The computer program product according to claim 15, wherein said XML specification includes custom scripting for form events.

17. The computer program product according to claim 16, wherein possible responses to a form event include hiding a question within said patient form and revealing a question within said patient form.

18. The computer program product according to claim 12, wherein said post-randomization form includes a randomization code for a patient of a clinical trial.

19. The computer program product according to claim 14, further comprising generated code deployable for use in any of an internet information server and an interactive voice response system.

20. The computer program product according to claim 10, further comprising code for restricting read and edit permissions to control who has what permission in relation to said patient form.